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STUDIES IN BIOMIMETIC ALKALOID SYNTHESES—9

TWO TOTAL SYNTHESES OF MINOVINCINE

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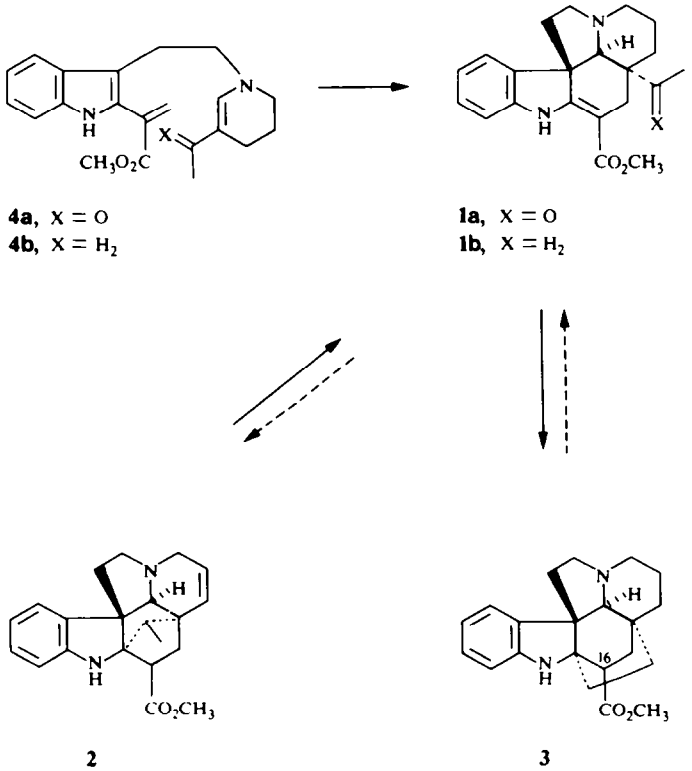
Abstract—Condensation of methyl 1,2,3,4,5,6-hexahydroazepino[4,5-b]indole-5-carboxylate (**5**) with the ethylene ketal of 2-acetyl-5-chloropentanal, followed by reactions with triethylamine and aqueous acid gave minovincine **1a**. Alternatively, a condensation of the indoloazepine hydrochloride **5a** with the sodium enolate of formyl acetone, followed by acid cyclization, N-benzylation and reaction with base gave the 19-oxosecodine analogue **13**. Thermal cyclization of the latter, debenzylation by hydrogenolysis, alkylation with 1,3-bromochloropropane and final cyclization gave minovincine **1a**. This sequence provides the first example of isolation and subsequent cyclization of a reactive secodine analogue.

The pentacyclic alkaloid minovincine (**1a**) constitutes a biogenetic link between the hexacyclic dihydroindole alkaloids of the vindolinine (**2**) and the kopsinine (**3**) classes of alkaloids (Scheme 1). Indeed, chemically minovincine (**1a**) has been obtained by fragmentation of natural vindolinine (**2**), followed by oxidative and reductive steps and minovincine (**1a**) has also been converted to 16-epikopsinine (**3**, 16α-carbomethoxy group) by acid catalysed cyclization and reduction.[1]

Since no synthesis of minovincine (**1a**) was known, it was of interest to see if our biomimetic strategy for construction of aspidosperma type alkaloids, which utilized secodine (**4b**) type intermediates,[2,3] could be extended to this biogenetic turntable **1a**,[4] and thus serve as a platform for syntheses of more complex hexacyclic alkaloids (i.e. **2** or **3**).

An extension of the concepts of our previous syntheses of vincadifformine (**1b**) and related alkaloids,[3,5-9] to a synthesis of minovincine (**1a**) would entail condensation of the carbomethoxy indoloazepine **5** with a 2-acetyl-5-halopentanal **6a** (Scheme 2). However, α-acyl aldehydes are known to undergo facile self-condensations (e.g. the spontane-



4a, X = O
4b, X = H_2

1a, X = O
1b, X = H_2

2

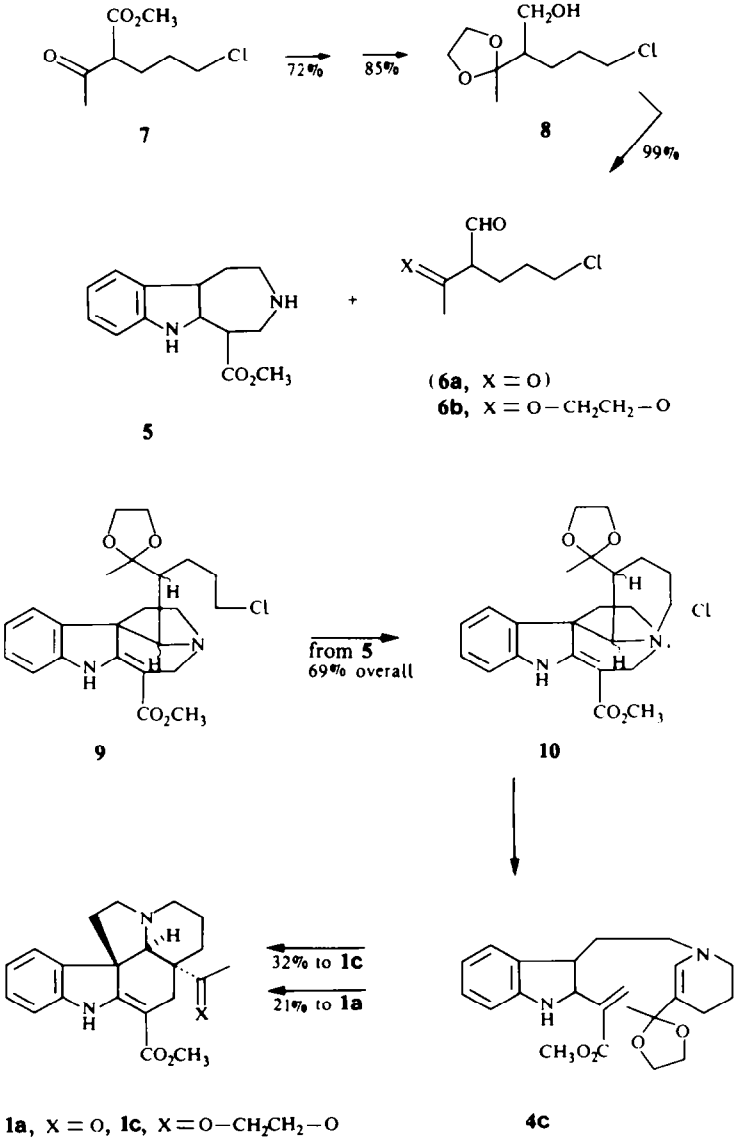
3

Scheme 1.

ous formation of triacetylbenzene from formylacetone). Thus corresponding synthons with a masked acetyl group or with a potential aldehyde function (see following paper) were required. An appropriate ketal aldehyde **6b** could be prepared, albeit in low yield, by alkylation of methyl acetoacetate with 1,3-chlorobromopropane, followed by ketalization of the β-keto ester **7** with ethylene glycol, reduction of the ester function with lithium aluminum hydride and final oxidation of the resultant alcohol **8** with pyridinium chlorochromate. A major problem with this sequence was cyclization of the desired acetoacetate C-alkylation product by subsequent O-alkylation, which reduced the yield of the initial product to 10%.[10]

Condensation of the indoloazepine **5** with the ketal aldehyde **6b** resulted in a mixture of four epimeric bridged azepines **9**, which underwent intramolecular quaternization. The initial intermediates **9** of these reactions and the following quaternary salts **10** could be identified by their characteristic UV absorptions (228, 290, 328 nm) as anilinoacrylates.[8] On treatment with triethylamine the quaternary salts **10** fragmented with transient formation of the secodine derivative **4c**. Instantaneous cyclization of this reactive intermediate then produced the minovincine ketal **1c**. Minovincine (**1a**) was obtained by hydrolysis of the ketal function with aqueous sulfuric acid. Since relatively strenuous conditions were required for the hydrolysis of this neopentyl ketal, partial destruction of the product resulted in a consequent low yield (21%) of the alkaloid from this last reaction.[11]

While a synthesis of minovincine (**1a**) has now been achieved, the low yield in the final ketal hydrolysis does not allow one to consider this minovincine synthesis as a starting point for the generation of other alkaloids. A further consideration for modification of this synthesis was the hope that it

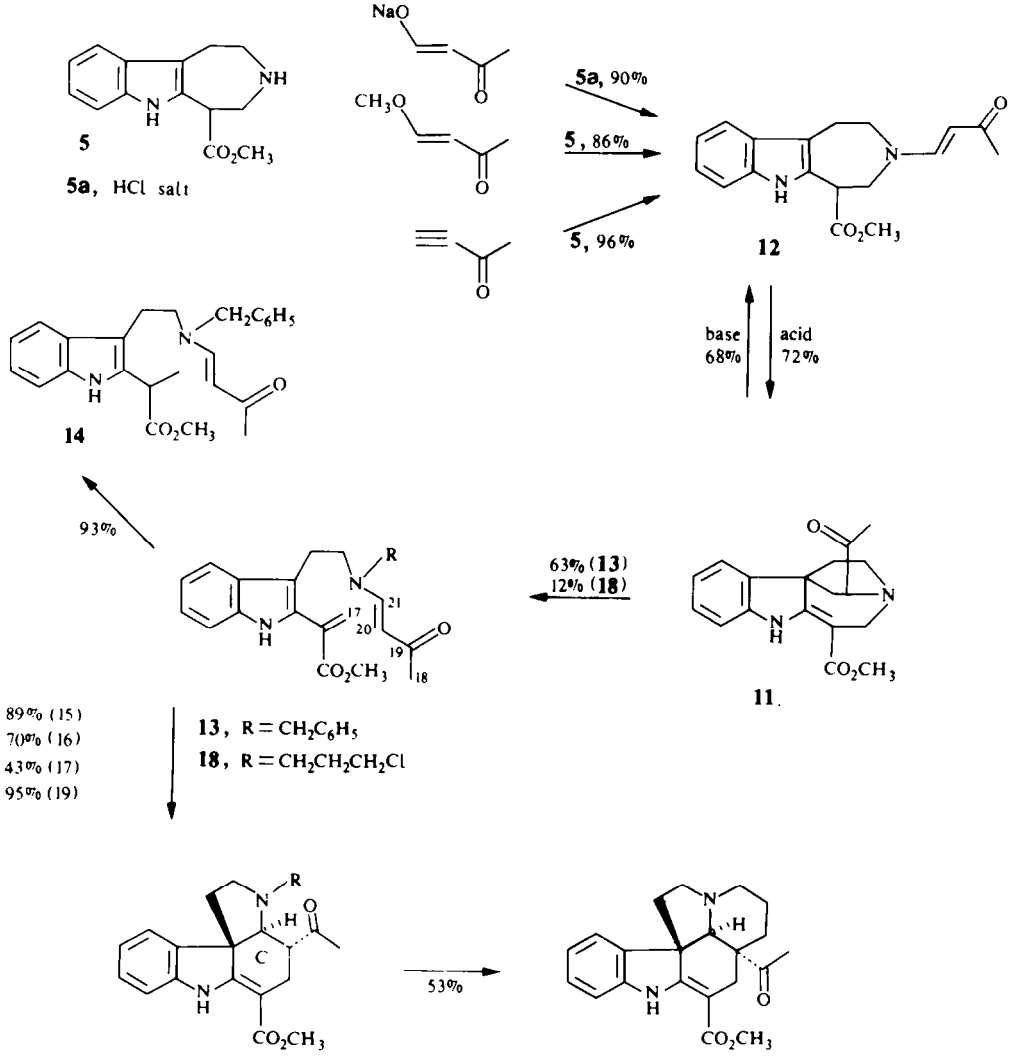


Scheme 2.

might lead to a 19-oxosecodine intermediate **4a** and that it would thus allow a study of the reactivity of this intermediate and its possible conversion to minovincine (**1a**).

In principle it might seem possible to hydrolyse the ketal function at the bridged azepine **9** or at the quaternary salt **10** stages of the synthesis. Subsequent fragmentation of a ketone equivalent of **10** should then yield the 19-oxosecodine **4a**. However, it was found that minovincine ketal **1c** could already be observed by TLC during the initial condensation of the indoloazepine **5** with the chloroaldehyde **6b**. Its rapid formation at that point can be attributed to a facile intramolecular quaternization of those two bridged indoloazepine epimers **9**, which have a proximate alkyl chloride chain and nitrogen unshared electron pair, rather than to the two epimers of **9** in which the alkyl chain extends over the acrylate moiety, with consequent slower rates of intramolecular quaternization.[8] The starting indoloazepine **5** and the intermediates **9** can then serve as bases to initiate fragmentation of the quaternary salts **10**, thereby forming the secodine 19-ketal intermediate **4c**.

The complexity of diastereomeric mixtures of **9** and **10**, with differential rates of ketal hydrolysis of their components and the aforementioned differential propensity of these components for spontaneous progression to minovincine ketal **1c** did not agur well for a clean formation and isolation of a 19-oxosecodine (**4a**). Moreover, it was found that condensation of the indoloazepine *hydrochloride* (**5a**) with the ketal aldehyde **6b** gave deacylated quaternary salts corresponding to **10** and subsequently deacylminovincine (desethylvincadifformine) rather than minovincine (**1a**) after treatment with base. The



Scheme 3.

synthesis of a 19-oxosecodine (**4a**) was consequently found to require an alternative approach (see following paper).

A second synthesis of minovincine (**1a**), which allowed a study of the reactivity of the characteristic vinylogous amide function with the indoloacrylate moiety found in a 19-oxosecodine (**4a**), was therefore undertaken. This synthesis also overcomes the disadvantage of starting with the poorly accessible ketal aldehyde **6b** and it avoids the low yielding minovincine ketal hydrolysis. It is based on our strategy of generating bridged indoloazepine intermediates by condensation of the indoloazepine **5** with simple aldehydes, followed by an intermolecular N-alkylation and molecular rearrangement.[8] To this end (Scheme 3) the indoloazepine hydrochloride **5a** was condensed with the sodium enolate of formyl acetone, avoiding with this procedure the normal rapid self-condensation of the formyl ketone. The product of this reaction was, however, not of the previously encountered bridged indoloazepine type **11**, but it was instead the vinylogous amide **12**, with UV absorption at 226 and 301 nm and with an NMR spectrum displaying two vinyl protons.

Alternatively, this condensation product could also be obtained from reactions of the indoloazepine **5** with ethynyl methyl ketone or with 4-methoxybut-3-ene-2-one.

On reaction with HCl in tetrahydrofuran the condensation product **12** cyclized to give the hydrochloride of the desired bridged indoloazepine **11** (UV 228, 290, 328 nm; NMR without vinyl protons). The free base of **11**, obtained on neutralization, was found to revert slowly to the initial vinylogous amide **12**. An equilibration favoring the olefinic product **12** under neutral or basic conditions, but yielding the bridged azepine **11** in acid, is readily understood in terms of the relative basicities and electronic stabilizations of these compounds (tertiary amine vs vinylogous amide).

On stirring with benzyl bromide the bridged indoloazepine **11** was quaternized. When the resulting salt was heated with triethylamine in methanol it fragmented and the indoloacrylate **13** was obtained as a stable, crystalline product with characteristic UV absorption at 231 and 311 nm.[12] Its NMR spectrum showed vinylogous amide *E*-vinyl protons at δ 7.61 and 5.27 (J = 13 Hz) as well as two acrylate methylene proton signals at δ 6.50 and 5.95. The latter signals were lost in the dihydro compound **14**, which was obtained by catalytic hydrogenation of the acrylate **13**.

An NMR spectrum of the vinylogous amide **13** at 190°K clearly showed the presence of four structures derived from rotation about the N to C-21 and about the C-20 to C-19 bonds of the acyl enamine, with four corresponding methyl groups seen in a ratio of 13:43:29:15 and with corresponding sets of vinyl doublets. These data correlate with spectra obtained with the analogue N-benzyl-N-methylbut-3-en-2-one, for which four rotational isomers, in a ratio of 16:54:6:24, were found at 210°K and they are in agreement with NMR studies of other examples of *E*-vinylogous amides.[13]

When the 19-oxosecodine analogue **13** was heated at reflux in toluene, it cyclized stereospecifically to form the tetracyclic amino ketone **15** in 89% yield. The N and acetyl functions in this product can be assigned as *trans* substituents on the unsaturated ring C (*vide infra*). This cyclization result follows from an intramolecular Diels–Alder addition of the indoloacrylate unit to the *E*-vinylogous amide function of **13** and it corresponds to analogous products obtained with previously studied basic secodine analogues lacking a piperideine ring.[8]

Inspection of the IR and H NMR spectra of the tetracyclic amino ketone **15** caused some initial consternation. The compound did not show carbonyl absorption above 1695 cm^{-1}, contrary to expectation for an unconjugated ketone.[14] The compound also showed a one proton singlet in its 250 MHz NMR spectrum at δ 3.72; a signal without parallel in spectra of analogous compounds with alkyl groups in place of the acetyl substituent.[8,15] These findings lead us to the proposal of conformational structure **15a**, with ring C forced into a quasi boat by repulsion of the N-benzyl and acetyl groups. Electronic interaction between the CO group and the anlinocyclohexene π system would produce the observed decrease in CO stretching frequency and result in restricted rotation of the acetyl group.[16] In the resulting acetyl rotamer where the CO oxygen points towards the proton of the N substituted methine, an anisotropic interaction would account for the pronounced downfield shift of this proton. Minimal coupling of the adjacent methine protons, with a relative *trans* configuration and near 90° dihedral angle, had already been seen in analogues of **15**, with alkyl groups in place of the acetyl function.[8] Thus a singlet at δ 3.72 (instead of one around δ 2.9) could be accounted for with structure **15a**.

Corresponding IR and NMR results were also obtained with an analogue of the amino ketone **15** where a Me substituent replaced the benzyl substituent on N.

Catalytic hydrogenolysis of the tertiary amine **15** provided the debenzylation product **16**. The secondary amine **16** showed a normal CO stretching frequency at 1708 cm^{-1} and lacked the δ 3.72 NMR singlet of the tertiary amine **15**. With loss of the N-alkyl substituent of **15** a conformational structure **16a** with ring C in a quasi chair conformation now becomes possible and N inversion is facilitated due to a diminished steric compression of the smaller N_b substituent against the aromatic ring A peri proton. As a result the acetyl group is freed in **16** from its previous interaction with the enamine double bond and with the methine proton in **15**. N-alkylation of the secondary amine **16** with 1,3-chloroiodopropane furnished the chloroketone **17**.

A more direct synthesis of the chloride **17** was obtained by N-alkylation of the bridged indoloazepine intermediate **11** with 1,3-chloroiodopropane (Scheme 3). Fragmentation of the resultant quaternary salt generated the indoloacrylate **18** and cyclization of the latter then produced the chloride **17**. While this synthesis was more direct than the sequence using benzylation and debenzylation steps, it was less effective. A slower alkylation of the bridged indoloazepine **11** by 1,3-chloroiodopropane, as compared with benzyl bromide, resulted in extensive rearrangement of the tertiary amine **11** back to its more stable precursor **12** (see above). Thus an effective elaboration of functionalized bridged in-

doloazepines such as **11** under neutral or basic conditions calls for relatively reactive alkylating agents.

For the final closure of ring D of minovincine (**1a**) an exchange of chloride for iodide on the chloroketone **17** was required. The chloroketone **17** was recovered unchanged from attempted cyclization with potassium t-butoxide at room temperature and it was destroyed at elevated temperatures. However the corresponding iodide, obtained with NaI in acetone in 95% yield, cyclized in a reaction with potassium t-butoxide at room temperature, giving minovincine (**1a**) in 76% yield.

The generation and secodine type cyclizations of the vinylogous amide intermediates **13** and **18**, which have been found in these studies, now supported the anticipation that a 19-oxo-Δ^{20}-secodine **4a** could serve as a direct precursor of minovincine (**1a**). The synthesis and reactivity of this biogenetic intermediate are described in the following paper.

EXPERIMENTAL

Methyl 2 - acetyl - 4 - chloropentanoate (**7**).[17] At 20°, 87.1 g (81 ml, 0.75 mol) methylacetoacetate was added to 27.0 g (0.50 mol) NaOMe in 250 ml MeOH. After heating for 10 min at reflux and cooling to −10°, 118.1 g (80.2 ml, 0.75 mol) 1-bromo-3-chloropropane was added rapidly. The mixture was heated at reflux until it was neutral to litmus, then cooled and concentrated under vacuum. Addition of 50 ml water, extraction with 3 × 150 ml CH_2Cl_2, concentration of the $MgSO_4$ dried extracts and distillation at 145–149° (20 mm) gave 10.1 g (10.5%) of the chloroester.

Ethylene ketal of methyl 2 - acetyl - 4 - chloropentanoate (**8**).[17b] With a Dean Stark water separator a mixture of 7.6 g (0.039 mol) of the above keto ester, 2.6 g (0.042 mol) ethylene glycol, 10 mg *p*-toluenesulfonic acid and 100 ml toluene was heated at reflux for 20 hr. The cooled mixture was shaken with 100 ml cold 10% NaOH and the aqueous layer extracted twice with 100 ml ether. Concentration of the $MgSO_4$ dried organic solns and distillation at 160–165° (20 mm) gave 6.7 g (72% yield) of the ketal ester. 100 MHz NMR ($CDCl_3$) δ 4.04 (s, 4H), 3.80 (s, 3H), 3.58 (t, 2H), 2.68 (t, 1H), 1.80 (m, 4H), 1.40 (s, 3H); IR (neat) ν_{max} 2950, 2890, 1735, 1430, 1380, 1353, 1266, 1205, 1135, 1040, 945, 870 cm^{-1}; TLC (silica, ether) R_f 0.69, (alumina, ether) R_f 0.65.

Ethylene ketal of 2-acetyl-5-chloropentanal (**6b**). At −10°, 4.3 g (0.018 mol) of the above ketal ester was added to 0.95 g (0.025 mol) LAH in 50 ml THF. After stirring for 1 hr at −10°, 8.1 g (0.025 mol) $Na_2SO_4 \cdot 10H_2O$ was slowly added, followed by 1 ml water. Vacuum filtration, washing of the solids with 100 ml ether, washing of the combined organic solns with satd brine, and extraction of the brine twice with 100 ml ether was followed by concentration of the combined ether solns. The residual ketal alcohol was found to decompose on distillation and was consequently purified by chromatography on alumina (Act. II–III), eluting 3.2 g (85% yield) with ether. 100 MHz NMR ($CdCl_3$) δ 3.99 (s, 4H), 3.76–3.46 (m, 4H), 3.28–2.90 (brd. m, 1H), 1.97–1.46 (m, 5H), 1.32 (s, 3H); IR (neat) ν_{max} 3420, 2920, 2860, 1430, 1373, 1201, 1030, 945, 863, 730 cm^{-1}; TLC (silica, ether) R_f 0.52, (alumina, ether) R_f 0.30.

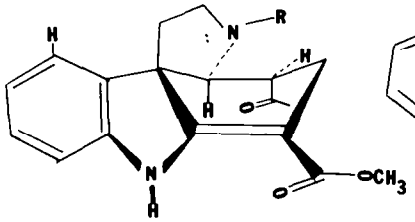
To a mixture of 0.113 g (1.39 mmol) NaOAc and 1.55 g (7.2 mmol) pyridinium chlorochromate in 10 ml dry CH_2Cl_2 was added dropwise a soln of 1.0 g (4.8 mmol) of the above ketal alcohol in 20 ml CH_2Cl_2. After stirring for 2 hr at 20°, 20 ml dry ether was added, and the soln filtered through 20 g Florisil. The residual material was washed with 3 × 20 ml ether and the combined filtrates concentrated to give 0.98 g (99% yield) of the chloroketal aldehyde; 100 MHz NMR ($CDCl_3$) δ 9.76 (d, 1H), 3.92 (s, 1H), 3.64–3.32 (m, 2H), 2.60–2.40 (m, 1H), 1.93–1.60 (m, 4H), 1.24 (s, 3H); IR (neat) ν_{max} 3040, 2960, 2830, 1715, 1490, 1425, 1256, 1191, 1085, 996, 920, 780 cm^{-1}; TLC R_f 0.74 (silica, ether).

Methyl 2-acetyl-4-benzyloxypentanoate, its ethylene ketal and 2-acetyl-4-benzyloxypentanol. A soln of 6.3 g (5.8 ml, 54 mmol) methyl acetoacetate and 8.3 g (8.1 ml, 54 mmol) 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in 100 ml benzene was stirred for 20 min and then 15 g (54 mmol) 3-iodopropyl benzyl ether was added at 20°. After 4 hr the mixture was washed with 50 ml water, the aqueous soln was extracted with two 100 ml portions ether and the combined organic solns were dried ($MgSO_4$) and distilled, providing 7.0 g (49%) of the alkylated ester; b.p. 148° (0.2 mm); 100 MHz NMR ($CDCl_3$) δ 7.28 (s, 5H), 4.28 (s, 2H), 3.72 (s, 3H), 3.48 (t, J = 6, 2H), 2.20 (s, 3H), 2.25–1.60 (m, 5H); IR (neat) ν_{max} 2940, 2850, 1738, 1715, 1615, 1490, 1449, 1430, 1355, 1215, 1195, 745, 695 cm^{-1}.

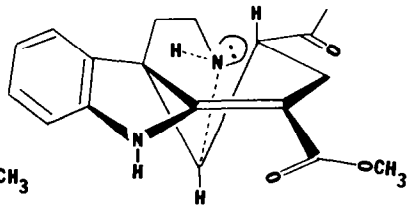
A soln of 7.0 g (26 mmol) alkylated acetoacetate, 1.9 g (1.7 ml, 30 mmol) ethylene glycol and 10 mg *p*-toluenesulfonic acid in 100 ml toluene was heated with a Dean–Stark water separator at reflux for 40 hr. The cooled soln was washed with cold 10% NaOH aq, the aqueous layer extracted twice with 100 ml ether and the combined organic solns were dried ($MgSO_4$) and distilled, giving 3.4 g (41%) of ketalester; b.p. 153° (0.2 mm). TLC (SiO_2, ether, detect. I_2) R_f 0.71; 100 MHz NMR ($CdCl_3$) δ 7.32 (s, 5H), 4.46 (s, 2H), 3.92 (d, 4H), 3.68 (s, 3H), 3.44 (t, 2H), 2.66 (t, 1H), 1.4–1.98 (m, 4H), 1.40 (s, 3H); IR (neat) ν_{max} 2920, 2860, 1730, 1445, 1350, 1200, 1030, 940, 870 cm^{-1}.

At −10° 3.4 g (11.0 mmol) of the above ketal was added to 0.95 g (25 mmol) LAH in 50 ml THF. After 3 hr 8.0 g (25 mmol) $Na_2SO_4 \cdot 10H_2O$ was added at −10°, followed by 1 ml water. The mixture was filtered and the solids were washed with 100 ml ether. The combined organic solns were washed with water and the water was extracted with three 100 ml portions ether. Concentration and chromatography of the residue on Woelm neutral alumina, Activity II–III, and elution with ether gave 2.65 g (86%) of the ketal alcohol; TLC, (alumina, ether) R_f 0.28, (SiO_2, ether) R_f 0.55; 100 MHz NMR ($CDCl_3$) δ 7.26 (s, 5H), 4.52 (s, 2H), 3.96 (s, 4H), 3.64 (t, 2H), 3.48 (t, 2H), 3.16 (t, 1H), 1.48–2.00 (m, 5H), 1.24 (s, 3H); IR (neat) ν_{max} 3400, 2940, 2880, 1450, 1375, 1210, 1153, 945, 870, 865, 734, 695 cm^{-1}.

Minovincine ethylene ketal (**1c**). To 1.00 g (4.09 mmol) of **5** in 20 ml THF was added 0.928 g (4.50 mmol) of **6b**. After 12 hr at 20° TLC (SiO_2, 4:1 EtOAc:ETOH, detection with cerric ammonium sulfate, CAS) showed R_f 0.70, aqua to blue to violet **1c** and an unidentified component staining brown, 0.57 blue to green **9**, 0.11 blue-grey **5** and 0, blue **10**. After 24 hr the R_f 0.57 spot for one set of epimers of **9** was



15a, R = $CH_2C_6H_5$ or CH_3



16a

missing and after 48 hr the starting azepine **5** had reacted completely. The soln was decanted from a red oil after 48 hr and the residual oil was triturated with 10 ml and 3 × 3 ml portions dry THF, producing 0.53 g of quaternary salts **10**. After further 48 hr an additional 0.69 g (69% total yield) of **10** was collected from the THF solns by this procedure; TLC (silica, MeOH (CAS) R_f 0, blue; UV of the THF solns of **9** and of the quaternary salts **10** *in* MeOH, λ_{max} 228, 290, 328 nm.

A mixture of 0.500 g (1.15 mmol) of **10**, five drops Et_3N and 10 ml acetonitrile was stirred at reflux for 24 hr. Concentration and partitioning between 5 ml of 10% NaOH aq and three 20 ml portions CH_2Cl_2, concentration of the organic solvent, and trituration with ether gave 0.145 g (32%) of **1c**, m.p. 162–164°; TLC (SiO_2, ether, CAS) R_f 0.43, aqua to blue to violet; UV (MeOH) λ_{max} 231, 305, 333 nm; 250 MHz NMR ($CDCl_3$) δ 8.94 (brd. s, 1H), 7.20–7.05 (m, 2H), 6.77–6.84 (m, 2H), 3.76 (s, 3H), 3.63–3.55 (m, 1H), 3.43 (q, J = 7, 14, 1H), 3.27 (q, J = 7, 14, 1H), 3.16–3.07 (m, 1H), 2.98–2.90 (m, 2H), 2.77–2.53 (m, 4H), 2.43–2.36 (m, 1H), 2.05–1.86 (m, 2H), 1.85–1.73 (m, 3H), 1.56–1.43 (m, 1H), 1.06 (s, 3H); IR (KBr) ν_{max} 3390, 2962, 2924, 2792, 1661, 1604, 1477, 1463, 1434, 1306, 1281, 1260, 1244, 1204, 1182, 1165, 1153, 1100, 1066, 1046, 1016, 877, 801, 739, 612 cm^{-1}; direct exposure probe mass spectrum (70 eV) *m/z* (rel. intensity) 397 (20), 396 (38), 381 (5), 309 (5), 183 (11), 182 (100), 168 (5), 167 (7), 154 (7), 138 (5), 123 (4), 110 (4), 96 (15), 87 (95). (Found: C, 69.42; H, 7.09; N, 6.86. Calc for $C_{23}H_{28}N_2O_4$: C, 69.68; H, 7.12; N, 7.06%).

Minovincine (**1a**) *from first synthesis.* A soln of 50 mg (0.12 mmol) of **1c** and 2 ml 20% H_2SO_4 in 5 ml MeOH was stirred for 18 hr at 20°. Partitioning between 10 ml 10% NaOH and there 20 ml portions of CH_2Cl_2, concentration of the organic extracts and centrifugal chromatography on silica with EtOAc furnished 9 mg (21%) of **1a** identified by NMR, UV, IR and TLC comparisons with the product obtained in the second synthesis (below).

Desacetylminovincine. A mixture of 500 mg (1.78 mmol) of hydrochloride **5a** and 335 mg (1.96 mmol) of **6b** in 10 ml MeOH was stirred at 20° for 3 days. TLC (SiO, 4:1 ETOAc:ETOH) then showed two bridged azepine products with R_f 0.73 (blue–green), major and 0.49 (blue–green), minor, a trace of rearranged compound with R_f 0.22 (blue) and a trace of **5** with R_f 0.06 (blue–grey). The solvent was evaporated under vacuum, and the residue partitioned between two 40 ml portions CH_2Cl_2 and 10 ml 10% NaOH aq. Concentration of the organic extracts and stirring of the residue in 40 ml THF for 12 hr led to deposition of 410 mg of quaternary salts. A direct insertion probe mass spectrum of this salt indicated a molecular ion at *m/z* 310 due to loss of the $C_4H_7O_2$ acyl ketal function and no peak at *m/z* 396. The latter ion was, however, observed with a sample of the quaternary salt **10**, obtained above. The salt was heated in 20 ml THF and three drops of Et_3N. Concentration and partitioning between CH_2Cl_2 and dil NaOH aq and concentration of the organic extracts showed that this yielded only desacetylminovincine, and no minovincine or minovincine ketal or other products in amounts which would allow isolation. The desacetylminovincine (desethylvincadiffor-mine) was identified by NMR, mass fragmentation and TLC comparison with an authentic sample.[8]

Methyl 3 - (4 - *but* - 3 - *ene* - 2 - *one* - *yl*) - 1,2,3,4,5,6 - *hexahydroazepino*(4,5-b)*indole* - 5 - *carboxylate* (**12**) *and methyl* 1,2,4,6 - *tetrahydro* - 11 - (3 - *propan* - 2 - *one* - *yl*)-3,5b - *methanoazepino*(4,5b)*indole* - 5 - *carboxylate* (**11**)

(a) The indoloazepine **5** was converted to its hydrochloride **5a** by addition of 4 ml ether, which had been saturated with HCl gas, to a soln of 5.40 g (0.0221 mol) of the azepine in 50 ml CH_2Cl_2. Evaporation of all solvents under vacuum, suspension of the residue in 50 ml ether and filtration gave the hydrochloride salt. This salt was stirred for 12 hr with 2.76 g (0.0256 mol) of the sodium enolate of formylacetone[18] in 100 ml THF. Concentration and partitioning between 30 ml water and 60 ml CH_2Cl_2, extraction with 60 ml CH_2Cl_2, concentration of the organic solns and chromatography of the residue on 200 g silica, eluting first with EtOAc and then with 5:1 EtOAc:EtOH for collection of the product, gave 6.23 g (90%) of amorphous enone **12**; UV (MeOH) λ_{max} 226, 301 nm; IR (KBr) ν_{max} 3203, 2943, 1727, 1642, 1582, 1542, 1436, 1355, 1270, 1155, 940, 740 cm^{-1}; 250 MHz NMR ($CDCl_3$) δ 8.69 (brd s, 1H), 7.65–7.64 (m, 1H), 7.49 (d, 1H), 7.21–7.08 (m, 3H) 5.29–5.19 (m, 1H), 4.19–3.45 (m, 5H), 3.85 (s, 3H), 3.19–3.00 (m, 2H), 2.13 (s, 3H); mass spectrum (80 eV) *m/z* (rel. intensity) 313 (16), 312 (66), 256 (12), 214 (100), 183 (15), 156 (43), 154 (34), 98 (33), 91 (21); TLC R_f 0.10 (silica, 2% MeOH in CH_2Cl_2, green with CAS spray), R_f 0.50 (silica, 4:1 Et-OAc:EtOH), R_f 0 (silica, 9:1 benzene:Et_3N).

(b) Alternatively, 0.835 g (12.0 mmol) 3-butyne-2-one was added to a soln of 2.00 g (8.19 mmol) of **5** in 25 ml acetonitrile. After 3 hr of stirring under N_2 at 20° the mixture was concentrated under vacuum and the residue chromatographed on 100 g silica, eluting with 5:1 EtOAc:EtOH, to provide 2.46 g (96% yield) of **12**.

(c) The same product was obtained in 86% yield from a 2 hr reaction of **5** with 4-methoxy-3-butene-2-one in acetonitrile at 20°.

To a soln of 2.0 g (0.64 mmol) of **12** in 40 ml THF was added 1 ml ether saturated with HCl gas. An initially formed cloudiness (HCl salt of **12**) disappeared in 30 min. After 60 min no **12** was detected by TLC. The solvent was removed under vacuum and the residue partitioned between 30 ml 10% NaOH and two 40 ml portions CH_2Cl_2. Concentration of the organic solns and column chromatography of the residue on 150 g silica, eluting with 9:1 benzene:Et_3N, and crystallization of the eluate from EtOAc gave 1.44 g (72%) of bridged **11**, m.p. 157–159° (this m.p. is actually that of the rearrangement product **16**, see below); UV (MeOH) λ_{max} 225, 298, 325 nm; IR (KBr) ν_{max} 3370, 2968, 2870, 1716, 1682, 1609, 1480, 1445, 1298, 1245, 1202, 1052, 785 cm^{-1}; 250 MHz NMR ($CDCl_3$) δ 8.97 (s, 1H), 7.27–7.18 (m, 2H), 7.15–6.83 (m, 2H), 3.98 (d, 1H), 3.72 (s, 3H), 3.56–3.45 and 3.45–3.34 (m, 3H), 2.79 (m, 3H), 2.40–2.21 (m, 2H), 2.35 (s, 3H); mass spectrum (80 eV) *m/z* (rel. intensity) 313 (64), 312 (100), 281 (14), 269 (10), 239 (16), 227 (23) 215 (79), 214 (100), 182 (51), 154 (79), 127 (46), 98 (52); TLC R_f 0.10 (silica, 2% MeOH in CH_2Cl_2, blue with CAS spray), R_f 0.42 (silica, 3:1 EtOAc:ethanol), R_f 0.42 (silica, 9:1 benzene:Et_3N). (Found: C, 68.97; H, 6.54; N, 8.73. Calc for $C_{18}H_{20}N_2O_3$: C, 69.21; H, 6.45; N, 8.96%).

A soln of 0.200 g (0.640 mmol) of bridged **11** in 6 ml benzene and 2 drops Et_3N was heated at reflux for 6 days. Concentration and column chromatography on 75 g silica, eluting with 5:1 EtOAc:EtOH gave 0.136 (68%) of **12**, identified by all spectroscopic and chromatographic criteria given above.

N - *Benzyl* - N - *methyl* - 4 - *aminobut* - 3 - *ene* - 2 - *one*. A mixture of 8.11 g (0.052 mol) N-benzylmethylamine hydrochloride and 5.99 g (0.055 mol) formylacetone sodium enolate in 25 ml CH_2Cl_2 was stirred for 2 hr at 20°. Partitioning with 20 ml water, extraction with 2 × 50 ml CH_2Cl_2, concentration and column chromatography on 200 g silica, eluting with 5:1 EtOH:EtOH gave 7.6 g (77%) of product with R_f 0.53 (silica, 4:1 EtOAc:EtOH); 250 MHz NMR at 296°K ($CDCl_3$) δ 7.69 (d, 1H), 7.39–7.17 (m, 5H), 5.16 (d, 1H), 4.38 (s, 2H), 2.73 (brd. s, 3H), 2.12 (s, 3H); at 210°K (1:1 $CDCl_3$:CD_2Cl_2) 7.86 (d, J = 12.5 Hz, 54% H), 7.78 (d, J = 12.5 Hz, 16% H), 7.59 (d, J = 13.2 Hz, 24% H) half of 4th doublet under aromatic protons, 6% H), 7.42–7.35 and 7.24–7.17 (m, 5 1/2H), 5.28 (d, J = 13.2 Hz, 16%H), 5.20 (d, J = 12.5 Hz, 54%), 5.20–5.13 (overlapping doublet, 6% H), 5.13 (d, J = 13.2 Hz, 24% H), 4.50, 4.46, 4.39, 4.37 (4s, 2H), 3.18, 3.12, 2.73 (3s, 3H), 2.24 (s, 24% of 3H), 2.21 (s, 6% of 3H), 2.14 (s, 54% of 3H), 2.07 (s, 16% of 3H).

Methyl 4 - *acetyl* - 3 - *benzyl* - 1,2,3,3a,4,5 - *hexahydro* - 7H - *pyrrolo*(2,3-d)*carbazole* - 6 - *carboxylate* (**15**). A soln

of 0.556 g (1.78 mmol) of amine **11** and 0.580 g (3.40 mmol) benzyl bromide in 9 ml THF was stirred at 20° for 12 hr and filtered. Suspension of the quaternary salt in THF and its collection by centrifugation was repeated four times, followed by washing with ether and drying under vacuum to yield 0.65 g (76%) of N-benzyl quaternary salt of **11**. UV (MeOH) λ_{max} 232, 298, 330 nm; IR (KBr) ν_{max} 3380, 2950, 1695, 1645, 1610, 1480, 1465, 1437, 1388, 1360, 1295, 1247, 1190, 1060, 760, 705 cm^{-1}; TLC $R_f = 0$ (silica, 4:1 EtOAc:EtOH, CAS blue).

A corresponding methiodide was formed under the same conditions, 99% yield.

A mixture of 0.300 g (0.620 mmol) of the benzbromide, 4 drops of Et_3N and 8 ml MeOH was heated at reflux for 2 hr. Concentration under vacuum and crystallization from EtOAc gave 0.249 g (83%) of **13**, m.p. 135–137° (this m.p. is actually that of the thermal cyclization product **15**, as seen by TLC of the melted sample which differs from that of **13** by a slightly higher R_f value; less than 10% of **15** was formed in MeOH at reflux for 12 hr). For **13**: UV (MeOH) λ_{max} 231, 311 nm; IR (KBr) ν_{max} 3140, 3020, 2938, 1713, 1580 (broad) 1435, 1353, 1263, 1225, 1180, 1155, 943, 870, 808, 793, 728, 695 cm^{-1}; 250 MHz NMR, 293°K ($CDCl_3$) δ 9.33 (s, 1H), 7.61 (m, broad, 1H), 7.47–7.28 and 7.23–7.06 (m, 9H), 6.50 (d, J = 0.86 Hz, 1H), 5.95 (d, J = 0.8 Hz, 1H), 5.27 (m, broad, 1H), 4.27 (s, 2H), 3.54 (s, 3H), 3.37 (m, 2H), 3.06 (t, 2H), 2.10 (s, broad, 3H); 190°K (CD_2Cl_2) δ NH: 9.59, 9.53, 9.51 (3s, 1H); at C-21: 7.80, (d, J = 12.5 Hz), 7.65 (d, J = 12.9) 6.81 (d, J = 13.3, fourth doublet obscured by aromatic protons; aromatic: 7.63–7.35 (m), 7.29–7.09 (m); at C-17: 6.56, 6.54, 6.52, 6.47 (4 apparent s) and 6.02, 5.94, 5.91, 5.88 (4 apparent s); at C-20: 5.19 (d, J = 12.9 Hz), 4.80 (d, J = 13.3 Hz), 5.49–5.28 peaks under CH_2Cl_2; 4.39, 4.34, 4.28, 4.24 (4 apparent s) OCH_3: 3.85, 3.84, 3.83 (3 s); at C-18: 2.23, 2.14, 2.00, 1.73 (4 singlets in ratio 13:43:29:15); mass spectrum (80 eV) *m/z* (rel. intensity) 402 (100), 387 (4), 371 (13), 359 (19), 343 (11), 332 (66), 311 (7), 269 (72), 227 (63), 214 (59), 195 (37), 189 (50), 188 (66), 167 (39), 154 (54), 134 (40), 91 (61). (Found: 74.33; H, 6.40; N, 6.96. Calc for $C_{25}H_{26}N_2O_3$: C, 74.60; H, 6.51; N, 6.96%).

The correpsonding N-methylacrylate, m.p. 123–124°, was formed in 12 hr at 60° in 55% yield.

A soln of 0.200 g (0.497 mmol) of **13** and one drop Et_3N in 5 ml toluene was heated at reflux for 12 hr. Concentration under vacuum and chromatography on 25 g silica, eluting with ether, and crystallization from ether gave 0.178 g (89% yield) of **15**; m.p. 138–139°. TLC R_f 0.67 (silica, EtOAc, blue with CAS), R_f 0.53 (with ether); UV (EtOH) λ_{max} 230, 299, 329 nm; IR (KBr) ν_{max} 3360, 2912, 2828, 1695, 1670, 1633, 1610, 1484, 1469, 1438, 1380, 1348, 1251, 1215, 1190, 1170, 1130, 860, 755, 743, 710 cm^{-1}; 250 MHz NMR ($CDCl_3$) δ 8.78 (s, 1H), 7.39–7.26 (m, 5H), 7.18–7.10 (m, 2H), 6.92–6.78 (m, 2H), 4.01 (d, J = 13.3 Hz, 1H), 3.80 (d, J = 13.3 Hz, 1H), 3.76 (s, 3H), 3.72 (s, 1H) 3.24–3.15 (m, 1H), 3.01–2.95 (m, 1H), 2.78–2.68 (m, 3H), 2.07–1.95 (m, 1H), 1.97 (s, 3H), 1.71 (d, d J = 4.5, 11.8 Hz, 1H); mass spectrum (80 eV) *m/z* (rel. intensity) 403 (48), 402 (100), 371 (13), 359 (14), 343 (7), 311 (7), 270 (48), 269 (78), 228 (34), 227 (65), 214 (53), 195 (30), 189 (48), 188 (69), 167 (36), 154 (39), 134 (46), 91 (66). (Found: C, 74.80; H, 6.60; N, 6.80. Calc for $C_{25}H_{26}N_2O_3$: C, 74.60; H, 6.51; N, 6.96%).

The corresponding N-methyl tetracyclic amino ketone, m.p. 174–175° was formed under the same conditions in 73% yield. The N-ethyl analogue had m.p. 140–141°.

N - *Benzyl* - N - (1 - *butene* - 3 - *oneyl*) - N - 2 - [3 - [2-[*methyl* - 2 - *propionyl*] - *indol*]*ethyl*] *amine* (**14**). A soln of 0.074 g (0.18 mmol) of **13** in 5 ml dry THF was stirred with 8 mg 10% Pd/C for 3 hr under H_2. Filtration, washing of the catalyst with hot MeOH, partitioning of the combined filtrates between water and CH_2Cl_2 and chromatography of the organic extracts on silica, eluting with EtOAc, gave 0.070 g (93%) of **13**. UV (MeOH) λ_{max} 228, 304 nm; IR (KBr) ν_{max} 3250, 3050, 2960, 1738, 1650, 1590, 1550, 1455, 1440, 1365, 1205, 1175, 965, 750 cm^{-1}; 250 MHz NMR ($CDCl_3$) δ 8.43 (s, 1H), 7.64 (brd. s, 1H), 7.32 (m, 5H), 7.13 (m, 4H), 5.28 (m, 1H), 4.22 (brd. s, 2H), 3.90 (q, J = 7.2 Hz, 1H), 3.68 (s, 3H) 3.31 (m, 2H), 2.93 (m, 2H), 2.14 (m, 3H), 1.52 (d, J = 7.2 Hz, 3H); mass spectrum (80 eV) *m/z* (rel. intensity) 404 (100), 393 (11), 381 (33), 343 (19), 331 (43), 293 (31), 281 (46), 243 (50), 229 (78), 214 (71), 188 (70), 181 (69), 156 (61), 131 (68), 91 (63), 69 (68).

Methyl 4 - *acetyl* - 1,2,3,3a,4,5 - *hexahydro* - 7H - *pyrrolo*(2,3-d)*carbazole* - 6 - *carboxylate* (**16**). A soln of 0.25 g (0.62 mmol) of **15** in 8 ml AcOH was hydrogenated over 0.025 g 10% Pd/C at atmospheric pressure over 2 hr. Filtration and washing of the catalyst with hot MeOH and concentration of the combined filtrates under vacuum gave a residue which was dissolved in 10 ml CH_2Cl_2. The soln was washed with iced NH_4OH, concentrated and the residue chromatographed on 50 g silica, eluting with 10:1 CH_2Cl_2:MeOH. Crystallization of the concentrated eluate from EtOAc gave 0.14 g (70% yield) of **16**, m.p. 161–162°. TLC R_f 0.41 (SiO_2, 9:1 CH_2Cl_2:MeOH, blue CAS); UV (EtOH) λ_{max} 230, 300, 330 nm; IR (KBr) ν_{max} 3305, 3147, 2963, 2865, 1708, 1682, 1592, 1434, 1415, 1306, 1273, 1248, 1210, 1183, 1122, 1105, 1092, 1061, 850, 742 cm^{-1}; 250 MHz NMR ($CDCl_3$) δ 8.88 (s, 1H), 7.27–7.13 (m, 2H), 6.94–6.80 (m, 2H), 4.20 (s, 1H), 3.76 (s, 3H), 3.28–3.11 (m, 3H), 2.77–2.75 (m, 1H), 2.62, 2.56 (d, d, J = 14.3, 15.6, 1H), 2.05 (s, 3H), 2.05–1.79 (m, 3H); mass spectrum (80 eV) *m/z* (rel. intensity) 312 (100), 281 (31), 269 (32), 253 (14), 237 (18), 227 (62), 215 (79), 214 (92), 209 (38), 195 (44), 194 (47), 182 (61), 167 (56), 155 (55), 154 (74), 140 (23), 128 (28), 127 (38), 115 (25), 98 (56), 43 (55). (Found: C, 69.04; H, 6.72; N, 8.67. Calc for $C_{18}H_{20}N_2O_3$: C, 69.21; H, 6.45; N, 8.97%).

Methyl 4 - *acetyl* - 3 - [3 - *chloropropyl*] - 1,2,3,3a,4,5 - *hexahydro* - 7H - *pyrrolo*(2,3-d)*carbazole* - 6 - *carboxylate* (**17**)

(a) A stirred mixture of 100 mg (0.320 mmol) of **16**, 50 mg (0.36 mmol) K_2CO_3 and 102 mg (0.500 mmol) 3-chloroiododopropane in 15 ml benzene was heated at reflux for 7 hr. The solvent was removed under vacuum and the residue chromatographed on 25 g silica, eluting 54 mg (43% yield) of **17** as an amorphous solid. TLC R_f 0.72 (silica, EtOAc, CAS blue); UV (MeOH) λ_{max} 231, 300, 331 nm; IR (KBr) 3375, 2947, 2919, 2798, 1704, 1676, 1608, 1479, 1465, 1435, 1384, 1361, 1344, 1278, 1252, 1204, 1184, 1159, 1120, 1103, 1083, 1054, 1032, 1018, 983, 804, 783, 743, 693 cm^{-1}; 250 MHz NMR ($CDCl_3$) δ 8.80 (s, 1H), 7.23–7.13 (m, 2H), 6.92 (t, J = 4.1, 1H), 6.81 (d, J = 7.7, 1H), 3.76 (s, 3H), 3.74–3.61 (m, 2H), 3.58 (s, 1H), 3.25–3.17 (m, 1H), 3.12–2.96 (m, 2H), 2.90–2.58 (m, 4H), 2.17–1.92 (m, 3H), 2.05 (s, 3H), 1.79, 1.75 (d, d, J = 4.8, 11.9, 1H).

(b) A soln of 3.00 g (9.60 mmol) of **11** and 3.80 g (19.0 mmol) 3-chloroiodopropane in 20 ml THF was stirred for 48 hr at 20°. The resulting ppt was collected by centrifugation and decantation of solvent, then washed repeatedly with THF and dried to provide 1.80 g (36% yield) of a quaternary ammonium iodide, m.p. 168–170°. TLC R_f 0 (silica, 4:1 EtOAc:EtOH, CAS blue); UV (MeOH) λ_{max} 234, 295, 329 nm; IR (KBr) ν_{max} 3379, 2964, 2944, 2875, 1707, 1653, 1612, 1481, 1467, 1456, 1440, 1396, 1351, 1314, 1299, 1286, 1243, 1183, 1143, 1118, 1101, 1082, 1072, 1055, 1043, 1003, 774, 761 cm^{-1}; NMR ($CDCl_3$–D_6DMSO) δ 9.47 (s, 1H), 7.37–7.23 (m, 2H), 7.04–6.94 (m, 2H), 5.21–5.17 (m, 1H), 4.74 (d, 1H), 4.43–4.22 (m, 3H), 3.99–3.65 (m, 2(3) H), 3.80 (s, 3H), 2.90–2.78 (m, 1H), 2.68–2.30 (m, 6 (5) H), 2.14 (s, 3H). (Found: C, 48.30; H, 5.13; N, 5.22. Calc for $C_{21}H_{26}ClI\ N_2O_3$: C, 48.81; H, 5.07; N, 5.47%).

A mixture of 16.9 g (3.17 mmol) of the above quaternary salt and 1 ml Et_3N in 20 ml MeOH was stirred at 55–60° for 6 hr. Concentration under vacuum and chromatography of the residue on 85 g silica and elution with EtOAc gave 0.42 g (34% yield) of **18**, m.p. 130–132°. Formation of the corresponding cyclization product **17** (below) could be seen by TLC during the above course of generation of **18**. For **18**: R_f 0.35 (silica, EtOAc, CAS purple); UV (MeOH) λ_{max} 277,

307 nm; IR (KBr) ν_{max} 3146, 3105, 2940, 1719, 1616, 1591, 1442, 1365, 1286, 1262, 1229, 1202, 1185, 1163, 1148, 1127, 735 cm^{-1}; 250 MHz NMR ($CDCl_3$) δ 9.07 (s, 1H), 7.56 (d, J = 7.7, 1H), 7.37 (d, J = 8.8, 1H), 7.24–7.11 (m, 3H), 6.55 (d, J = 0.8, 1H), 6.04 (s, 1H), 5.21–5.06 (m, 1H), 3.88 (s, 3H), 3.58–3.33 (m, 4H), 3.25 (t, J = 6.9; 2H), 3.11 (t, J = 7.3, 2H), 2.18–1.85 (m, 5H).

A soln of 400 mg (1.03 mmol) of **18** and 0.5 ml Et_3N in 15 ml toluene was stirred at reflux for 26 hr. The concentrated mixture was then chromatographed on 50 g silica. Elution with EtOAc gave 220 mg (55% yield) of **17**, identical in all spectroscopic properties with the product obtained in section (a) above.

Minovincine (**1c**) *from second synthesis.* A mixture of 885 mg (2.20 mmol) of **17** and 3.41 g (22.8 mmol) NaI in 25 ml acetone was stirred at reflux for 12 hr. Concentration under vacuum and partitioning of the residue between three 25 ml portions CH_2Cl_2 and 10 ml water and concentration of the organic extracts gave **19** which was purified by chromatography through 20 g of SiO_2, eluting 0.96 g (95%) of amorphous compound with ether. TLC (SiO_2, ether, CAS) R_f 0.5, blue–purple; UV (MeOH) λ_{max} 224, 300, 329; 250 MHz NMR ($CDCl_3$) δ 8.80 (brd. s, 1H), 7.23–7.12 (m, 2H), 6.94–6.88 (m, 1H), 6.81 (d, J = 7.7, 1H), 3.76 (s, 3H), 3.57 (s, 1H), 3.36–3.31 (m, 1H), 3.32 (d, J = 5.8, 1H), 3.21 (dt, J = 2.4, 15.9, 1H), 3.07 (dd, J = 6.3, 8.7, 1H), 2.95–2.87 (m, 2H), 2.77–2.57 (m, 2H), 2.65 (dd, J = 3.97, 15.7, 1H), 2.10–1.93 (m, 3H), 2.06 (s, 3H), 1.76 (dd, J = 4.8, 11.9, 1H); IR (KBr) ν_{max} 3367, 2899, 2796, 1703, 1677, 1632, 1609, 1479, 1466, 1435, 1279, 1166, 1122, 1082, 745; direct exposure probe mass spectrum (70 eV) *m/z* (rel. intensity) 481 (21), 480 (65), 449 (6), 410 (12), 270 (20), 269 (100), 267 (11), 266 (95) 228 (11), 227 (72), 215 (11), 214 (88), 212 (29), 195 (30), 194 (32), 193 (11), 182 (16), 181 (11), 180 (17), 169 (10), 168 (24), 167 (42), 166 (21), 154 (44), 146 (12), 140 (21), 124 (14), 96 (26).

To a soln of 0.98 g (2.0 mmol) of **19** in 25 ml of t-BuOH, 0.63 g (6.0 mmol) t-BuOK was added and the yellow soln stirred at 20° for 12 hr. A second portion of 0.15 g (1.4 mmol) of the base was then added and stirring continued for 12 hr. Partitioning the mixture between 50 ml water and three 100 ml portions of CH_2Cl_2, concentration of the organic extracts and centrifugal chromatography on SiO_2, eluting with ether, gave 383 mg (53%) of d,l **1a**, m.p. 141–142°, crystallized from ether. TLC (SiO_2, ether, CAS) R_f 0.40, blue–violet); UV (MeOH) λ_{max} 224, 301, 329 nm; 250 MHz NMR ($CDCl_3$) δ 8.77 (brd. s, 1H), 7.31 (d, J = 7.3, 1H), 7.12 (dt, J = 1.2, 7.6, 1H), 6.92 (dt, J = 0.88, 7.7 1H), 6.77 (d, J = 7.7, 1H), 3.77 (s, 3H), 3.26 (d, J = 1.74, 1H), 3.16–3.09 (m, 1H), 3.06 (d, J = 15, 1H), 2.96 (dd, J = 6.3, 8.2, 1H), 2.80 (dd, J = 2.0, 15, 1H), 2.75–2.67 (m, 1H), 2.47 (dt, J = 2.9, 11, 1H), 2.01–2.18 (m, 3H), 1.88 (s, 3H), 1.76 (dd, J = 4.2, 11.4, 1H), 1.66–1.60 (m, 1H), 1.42 (dd, J = 5.1, 13, 1H); IR (KBr) ν_{max} 3372, 2939, 2924, 2777, 1699, 1667, 1607, 1478, 1465, 1434, 1253, 1238, 1199, 1149, 743 cm^{-1}; direct insertion probe mass spectrum (70 eV) *m/z* (rel. intensity) 353 (14), 352 (42), 321 (4), 309 (27), 293 (4), 265 (5), 249 (3), 214 (21), 206 (5), 139 (22), 138 (100). These data match those of corresponding spectra taken with samples of l-minovincine provided by Prof. Louisette Le Men and Prof. Geoffrey Cordell. (Found, C, 71.37; H, 6.86; N, 7.88. Calc. for $C_{21}H_{24}N_2O_3$: C, 71.57; H, 6.86; N, 7.95%).

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